UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,885	01/06/2006	Weihong Xie	0643418	8347

140 7590 12/28/2009

LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER
KASSA, TIGABU

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
12/28/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No.	Applicant(s)	
	10/542,885	XIE ET AL.	
	Examiner	Art Unit	
	TIGABU KASSA	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-18* is/are pending in the application.

4a) Of the above claim(s) *13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-12 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed November 16, 2009. **Claims 2-18 are pending. Claims 2-12 and 18 are under consideration in the instant office action**. Claims 13-17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claims.

Request for continued examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/16/09 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

Claims 2-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gai et al. (CN1273114, IDS reference) in view of Su et al. (US Patent 4,968,675).

Applicant Claims

Applicant claims a panax notoginseng saponins intravenous injection composition prepared by the steps recited in instant claim 18.The dependent claims thereof recite concentration of saponins, amount and types of iso-osmotic solution, and amount and types of pH-stabilizers.

Note: Instant claim 18 is written in a product-by-process format. The examiner takes the position that from the steps that are recited in the claim the structure of the claimed product is not different from the prior art product. The examiner notes that out of the steps recited filtering and boiling the solution may structurally change the composition. However, Gai et al. as set forth below clearly also teach filtering of the notoginseng saponin solution. Moreover, the compositions of the instantly claimed invention, for example, the examples applicant incorporated in the original specification experiments 1-5 (pages 4-7) clearly show that

applicant's process includes boiling and also pasteurization at 110 °C. The incorporation of both the boiling and pasteurization steps in applicant's disclosure is sufficient evidence that the compositions are not structurally affected either by boiling or pasteurization. As a result, the inclusion of the boiling steps by Gai et al. would not result in a structurally different product. With respect to the other steps, for example, mixing the notoginseng saponin powder with a diluted iso-osmotic solution, adding pH stabilizer, and making a diluted final product to a certain concentration would not result in a structurally different product because regulating pH and diluting the concentrated powder are clearly taught by Gai et al. as set forth below. Additionally, the incorporation of an iso-osmotic solution is rendered obvious by the combination teachings of Gai et al. and Su et al. Therefore, the product as instantly claimed is obvious and the steps recited in the claim would not result in a structurally different product. The examiner also points to a more depth explanation as set forth below in the body of the rejection.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Gai et al. teach an injection containing saponin powder of notoginseng, and water wherein the pH is regulated (see abstract). Gai et al. teach a refined injection is prepared through decocting notoginseng twice; merging filtrates, concentrating, adding alcohol; filtering by resin column then cold storage; recovering alcohol; filtering with Millipore filter membrane, regulating pH, concentrating, and drying to obtain total saponin powder of notoginseng; mixing it with the injection water, regulating pH value; boiling the solution, adding activated carbon; filtering and fine-filtering to obtain the product (see abstract).

Ascertainment of the Difference between Scope the Prior Art and the Claims (MPEP §2141.012)

Gai et al. do not teach the inclusion of an iso-osmotic solution. Gai et al do not teach how the pH of the injection is regulated. Gai et al do not specify concentration of the components. These deficiencies are cured by Su et al.

Su et al. teach a parenteral pharmaceutical composition comprising an active ingredient, citric acid, sodium citrate, sodium chloride, and water (column 1, lines 38-49). The concentration of sodium citrate is 0.05-6.4 mM (column 1, line 45). The examiner calculates that this corresponds to a sodium citrate concentration of 0.0118-1.5 mg/ml assuming disodium citrate. The sodium chloride concentration is 3-5 mg/ml (column 1, line 46). The sodium citrate/citric acid is used to optimize pH and the sodium chloride is used to optimize osmolality of the composition (column 1 line 66-column 2 line 2).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to stabilize the pH of a pharmaceutical composition for intravenous injection using, e.g., sodium citrate, because it is a known physiological buffer. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Furthermore, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Optimization of the concentration of the buffer is within the purview of the skilled artisan. The

skilled artisan would have been motivated to buffer the pH because unbuffered parenteral pharmaceutical compositions can cause hemolysis (Su et al., column 1 lines 61-63). The skilled artisan would have had a reasonable expectation of success in combining Gai et al. and Sui et al. because Su et al. teach the use of sodium citrate to buffer the pH of a parenteral pharmaceutical composition (column 1, lines 61-63) and Gai et al. teach regulating the pH of the solution. Additionally, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include an iso-osmotic solution in a parenteral pharmaceutical composition because the osmolarity of the aqueous pharmaceutical composition might otherwise be significantly lower than blood. Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). Optimization of the concentration of the iso-osmotic solution is within the purview of the skilled artisan. The skilled artisan would have been motivated to adjust the osmolarity of the parenteral pharmaceutical composition using, e.g., sodium chloride in order to avoid hypotension (Su et al., column 1 line 65-column 2, line 2). The skilled artisan would have had a reasonable expectation of success in adjusting the concentration

of the iso-osmotic solution because Su et al. teach the use of sodium chloride to adjust the osmolarity of a parenteral pharmaceutical composition (column 1 line 65-column 2, line 2). Additionally, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Applicants Remarks

Applicant's arguments filed on 11/16/09 have been fully considered but they are not persuasive. Applicants assert that there is no basis for turning to the teachings of Su et al. to address the deficiencies of Gai et al. The examiner reminds applicant that the rejection is based on the combined teachings of Gai et al. and Su et al. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375

(Fed. Cir. 1986). The examiner brought Su et al. in the rejection for curing the deficiencies of Gai et al. for not teaching the inclusion of an iso-osmotic solution, how the pH of the injection is regulated, and for not specifying concentration of the components not for the saponin powder of notoginseng. For Su et al. to be an appropriate prior art, Su et al. do not necessarily have to teach the saponin powder of notoginseng. Because Su et al. teach the use of an iso-osmotic solution and pH regulator and their concentrations in formulating similar pharmaceutical formulation, it would have been obvious to one of ordinary skill in the art to apply the teachings of Su et al. to the composition of Gai et al. Although the compound taught by Su et al. is not the same as the instantly claimed compound (i.e. the compound taught by Gai et al.), it is sufficiently similar as to provide valuable and relevant guidance to the skilled artisan in determining the types and amounts of buffers to use. Moreover, the teachings of Su et al. also lead the skilled artisan to include sodium chloride to adjust the osmolarity. Applicant also asserts that Gai et al. includes a boiling step, however, the compositions of the instantly claimed invention are not heated during preparation. This is not found persuasive because the compositions of the instantly claimed invention, for example, the examples applicant incorporated in the original specification experiments 1-5 (pages 4-7) clearly show that applicant's process includes boiling and also pasteurization at 110 ^{o}C. The incorporation of both the boiling and pasteurization steps in applicant's disclosure is sufficient evidence that the compositions are not structurally affected either by boiling or pasteurization. As a result, the inclusion of the boiling steps by Gai et al., would not result in a structurally different product. Furthermore, although boiling and pasteurization are not strictly synonyms, pasteurization according to Merriam-Webster's Online Dictionary is the partial sterilization of a substance and especially a liquid (as milk) at a

temperature and for a period of exposure that destroys objectionable organisms without major chemical alteration of the substance. Therefore, boiling constitutes a means of pasteurization. Moreover, the boiling/pasteurization is not expected to result in any structural differences in the composition and therefore is a process limitation which does not further limit the scope of the invention. With regard to the pH stability of the compositions, the examiner has pointed out Gai et al. teach the regulation of pH, although the means and the final pH are not cited in the abstract. Therefore, even without the teachings of Su et al., the regulation of pH is known and taught by Gai et al. Use of a physiological buffer for such a regulation would have been obvious to the skilled artisan since the composition of Gai et al. is designed for injection. The examiner further notes that the optimization of pH is within the purview of the skilled artisan and is, therefore, both obvious and reasonably expected to succeed. The teachings of Su et al. provide sufficient guidance to the skilled artisan to add appropriate physiological buffer and sodium chloride to the composition of Gai et al. since the compounds taught by Gai et al. and Su et al. are related steroid derivatives. By simply optimizing the pH and concentrations of buffer and salt, the skilled artisan would obtain pH stable composition. In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Claims 2-12 and 18 are rejected, while claims 13-17 remain withdrawn. Claim 1 is cancelled. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne P. Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa 12/11/09
/YVONNE L. EYLER/

Supervisory Patent Examiner, Art Unit 1619